

### REMARKS

Claims 1, 5-7, 9-10, 13-15, 17-18, 20-21 and 23 are presently pending in the instant Application. In the instant Amendment, Applicants have amended Claims 1 and 18, and have canceled Claim 23, without prejudice. Support for amended Claims 1 and 18 can be found generally throughout the instant Specification, and particularly on page 1, lines 33-38.

Applicants also file herewith a Notice of Appeal to the Board of Patent Appeals and Interferences (the "Notice"), and have attached a courtesy copy of the Notice hereto for the Examiner.

### *Claim Objections*

Claim 23 is objected to under 37 CFR 1.75. The Examiner has asserted that Claim 23 is a substantial duplicate of pending Claim 9. It is the Examiner's position that when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim.

In the instant Amendment, Applicants have canceled Claim 23, without prejudice. Hence, this objection is MOOT.

### *The Invention is Definite*

Claims 1,5-7, 9, 10, 13-15, 17, 20 and 23 remain rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the Invention. The Examiner had asserted the term "phenotyping" recited in Claim 11 lacks clarity. However, Applicants had previously canceled

Claim 11, and the Examiner has withdrawn this rejection of Claim 11.

The Examiner had also asserted the phrase “modified expression” recited in Claim 5 is indefinite. However, Applicants previously amended Claim 5 such that “modified expression” refers to the expression in step (a) of Claim 1. The Examiner has found that amendment persuasive, and has withdrawn this rejection of Claim 5.

The Examiner had also previously rejected Claim 12 for lacking clarity as to why an artisan would reduce gene expression in the control organism. However, Applicant previously canceled Claim 12, and the Examiner has withdrawn this rejection.

The Examiner also notes that the previous rejection of Claims 3, 4, 8, 11 and 12 under 35 USC § 112, second paragraph are withdrawn since Applicants previously canceled these Claims.

The Examiner has also asserted the phrase “perceptible from the outside” recited in Claim 1 is indefinite. The Examiner has asserted that previously Applicants indicated that the phrase refers to any modification or alteration of the yeast organism that can be measured on or outside of the modified organism and distinguishable from a wild-type unmodified yeast. The Examiner has also asserted that Applicants indicated on page 7, lines 13-17 of the instant Specification sets forth that analysis can “in principle include any modifications of the mRNA or protein steady state (transcription, translation, stabilization, etc.) and thus may also be carried out by protein profiling as well as the aid of lacuna protein assays”. It is the Examiner’s position that “physical” (e.g. size, shape, growth, or rate of cell division, see page 1, lines 33-38 of the instant Specification) and “non-physical attributes” such as secreted proteins, are encompassed by the Specification and the term “perceptible from the outside” recited in Claim 1. It is the Examiner’s

position though that this response does not clarify the metes and bounds of the claimed invention.

Although the Examiner has admitted that Applicant has clarified what is encompassed by a “perceptible” phenotype, wherein the term encompasses characteristics that can be detected by the naked eye and by an instrument (e.g. a tool that detects secretion of growth factor from a cell or microarray results that detect changes in gene expression), the Examiner believes Applicant’s previous response raises the question of how step (a) of Claim 1 is carried out. The Examiner contends that in step (a) of Claim 1, an artisan needs to select yeast that comprise a transgene which does not produce a detectable change of the phenotype which is perceptible from the outside of the yeast. However, the Examiner believes that all yeast comprising a transgene will produce a detectable change in their phenotype, as detection of phenotype, according to the Examiner’s interpretation of Applicant’s previous response, includes changes in gene expression that compensate for the changes caused by the transgene (see specification, page 2, line 38 to page 3, line 8). Hence, the Examiner contends that, given the metes and bounds of what is encompassed by “phenotype” it is unclear how artisan would arrive at any yeast that have no change in phenotype following introduction of a foreign gene into the yeast.

Applicant respectfully traverses this rejection. Initially Applicants note that Claim 23 has been canceled, without prejudice. Hence, this rejection of Claim 23 is MOOT. In the instant Amendment, Claim 1 has been amended such that a detectable change of the phenotype of the genetically modified yeast organism for drug screening that is perceptible from the outside of the yeast organism comprises the behavior of the yeast organism, the morphology of the yeast organism, or a combination thereof. Claim 18 has been amended to

be directed towards, *inter alia*, a genetically modified yeast, having genetically modified expression of at least one endogenous or foreign gene phenotype caused by the reduction or elimination of the compensating differential expression of the gene, wherein the phenotype of the yeast is perceptible from the outside of the yeast and comprises behavior of the yeast, the morphology of the yeast, or a combination thereof. Support for these amendments can readily be found on page 1, lines 24-38 of the instant Specification. Hence, this rejection should be withdrawn.

#### ***The Invention is Novel***

Claims 1-9, 10, 17, 28, 20, 21, and 23 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Chattopadhyay *et al.*, Journal of Bacteriology 182:6418-6423 (2000). The Examiner has asserted that Applicants indicate that in the previously filed Amendment, Claim 1 had been amended such that the heterologous expression of at least one protein fragment occurs as a result of introducing a foreign gene into the yeast organism, and that support for amended Claim 1 can be found in the instant Specification at page 4, line 27. However, the Examiner believes the previously made amendment to Claim 1 is not persuasive. The Examiner has asserted that yeast used in the experiments of Chattopadhyay *et al.* are btl 1 knockout yeast, wherein the knockout is made by homologous recombination (see Pearce and Sherman, 1997, Yeast 13:691- 697 (1997 (Fig. 1))). It is the Examiner's belief that the recombination construct contains an HIS3 reporter gene, wherein the HIS3 is expressed by the yeast, and the yeast do not exhibit a detectable change in their phenotype perceptible from the outside of the yeast.

Furthermore, the Examiner notes that while a rejection under 35 USC § 112 has been made in the instant Office Action, the Examiner maintains the instant rejection under 35 U.S.C. § 102(b). The Examiner has asserted it is understood from a strict reading of the instant Specification that the yeast selected in step (a) of pending Claim 1 are yeast that have no readily apparent phenotype. The Examiner's position is that Chattopadhyay *et al.* is readable on the claimed Invention since, in the Examiner's opinion, Chattopadhyay *et al.* teach that *btn1* knockout yeast have no readily apparent phenotype and a phenotype was detected following disruption of *btn2* and *hsp30* in *btn1* disrupted yeast. Hence, the Examiner has maintained this rejection.

The Examiner has also withdrawn the previous rejection of Claim 5 since nothing in Pearce and Sherman indicates the His gene was driven by an inducible promoter. In addition, the Examiner has withdrawn a previous rejection of Claims 3, 4, 8 and 11 under 35 U.S.C § 102(b) since Applicant has canceled those Claims.

Applicant respectfully traverses these rejections. Initially, Applicants note that Claim 23 have been canceled, without prejudice. Hence this rejection of Claim 23 is MOOT. With respect to Amended Claim 1, it comprises 3 steps:

a) causing heterologous expression of at least one protein or protein fragment by genetic modification by introducing a foreign gene into said yeast wherein the expression does not produce a detectable change of the phenotype which is perceptible from the outside of said yeast organism, wherein the detectable change of the phenotype which is perceptible from the outside of the yeast organism comprises the behavior of the yeast organism, the

morphology of the yeast organism, or a combination thereof;

b) analyzing the modified gene expression pattern and identifying compensating differentially regulated genes; and

c) phenotyping said yeast wherein phenotyping is carried out following the reduction or elimination of compensating differential expression which is perceptible from the outside of said yeast.

The Examiner has asserted that Chattopadhyay *et al.* is readable on the instant Invention since, in the Examiner's opinion, Chattopadhyay *et al.* teach that *btn1* knockout yeast have no readily apparent phenotype and a phenotype was detected following disruption of *btn2* and *hsp30* in *btn1* disrupted yeast. However, the Examiner is silent in asserting Chattopadhyay *et al.* teach *all* of the steps of pending Claim 1 because there is no teaching or suggestion of amended Claim 1 in Chattopadhyay *et al.* Indeed, at best, Chattopadhyay *et al.* can merely speculate that "...*perhaps* altered gene expression and modified vacuolar biochemistry contribute, at least in part, to maintaining a balanced cytosolic pH and maintaining cytosolic and vacuolar pH is important..." and thus is normalized in the strains in which genes are deleted to that found in a wildtype strain (emphasis added). However, and most importantly, Chattopadhyay *et al.* go on to explain "[c]learly this study has *not* completely addressed how *btn1*-Δ, with *btn2*-Δ and *hsp30*-Δ mutations, balances vacuolar

pH (emphasis added). Thus, Chattopadhyay *et al.* have no teachings that a genetically modified yeast organism that is caused to express heterologously at least one protein or protein fragment by genetic modification by introducing a foreign gene into the yeast wherein the expression does not produce a detectable change of the phenotype, which is perceptible from the outside of said yeast organism as set forth in Amended Claim 1, would even have a modified gene expression pattern to be analyzed. MPEP § 706.02 clearly states that "...for anticipation under 35 U.S.C. 102, the reference must teach *every aspect of the claimed invention either explicitly or impliedly*. Any feature not directly taught must be inherently present (emphasis). Since Chattopadhyay *et al.* clearly do not teach every aspect of the instant Invention either explicitly or impliedly, the instant Invention is clearly novel over the teachings of Chattopadhyay *et al.*, and this rejection should be withdrawn.

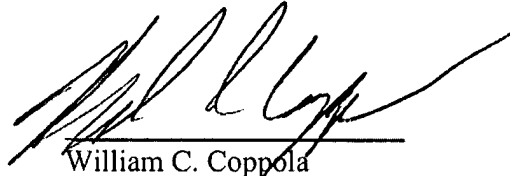
*Fees*

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,



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